rather than nasal colonization with MRSA—may be a better predictor of children at higher risk of subsequent SSTI.

One of the major limitations of this study is that only the anterior nares was cultured to evaluate colonization. Other studies have identified carriage of Staphylococcus aureus in the pharynx, axilla, perineum, and the skin. Nonetheless, the anterior nares is consistently the most common single site for detecting colonization, and is the method most commonly used for detection of colonization status. Other limitations of this study include a small sample size; incomplete follow-up on some patients; incomplete information regarding infection and colonization in household members; and current lack of information about the antibiotic used for treatment in this blinded trial.

Children presenting with SSTIs have higher rates of S. aureus nasal colonization than healthy counterparts, but there is substantial discordance between wound and nasal strains. SSTI recurrence after incident MRSA infection was very common overall in our study, but baseline MRSA nasal colonization status did not help to predict children at risk for recurrent SSTIs. The utility of determining nasal colonization status in children with CA-MRSA infections remains uncertain.

REFERENCES

older children. The 2 NRTIs used in the efavirenz-based regimen were stavudine (15- and 30-mg capsules or syrup; TGPO) and lamivudine (150-mg tablets or syrup; TGPO). The dosages of stavudine and lamivudine were calculated as 1 and 4 mg/kg q12 hours, respectively. The method of using divided adult FDC in pediatric patients at our institute has been reported.10

Children were assessed at week 0, 4, 8, 12, and every 12 weeks thereafter. The rate of adherence was defined as the number of doses taken divided by the total number of doses prescribed. Returned medication was counted and caregiver interviewed. Poor adherence was defined as an adherence rate of <95% recorded at any scheduled visit. Weight and height were expressed as weight-for-age and height-for-age z scores. CD4 cell percentages and plasma HIV RNA level were performed at baseline and every 24 weeks thereafter. The study and informed consent form were approved by the research ethics committee of Chiang Mai University.

Statistical Analysis. Immune recovery was defined as CD4 cell percentage ≥25%. Virologic suppression was defined as plasma HIV RNA level <400 copies/mL. Patients who died or discontinued NNRTI-based treatment regimen were counted as virologic failure. Their subsequent CD4 cell percentage values were assumed to be <25%. Comparison of variables was performed using Student t test or Fisher exact test as appropriate. Data were analyzed with the SPSS version 11.5 (SPSS Inc., Chicago, IL). A 2-sided P value < 0.05 was considered significant.

RESULTS

Twenty-six children met the eligibility criteria. Thirteen (50%) were male. Nineteen (73%), 3 (12%), and 2 (8%) were in WHO clinical stage 4, 3, 2 and 1, respectively. The median age at HAART initiation was 9.8 months (range, 1.5–24.0). The median body weight was 6.7 kg (range, 4.1–11.5). Treatment characteristics are summarized in Table 1. The median baseline plasma HIV RNA was 4.9 log_{10} copies/mL (range, 3.9–9.9). Thirteen children (50%) had baseline plasma HIV RNA >750,000 (5.9 log_{10}) copies/mL.

Twenty children (77%) had a history of exposure to antiretroviral drugs to prevent mother to child transmission (PMTCT). Four had been exposed to zidovudine and nevirapine (3 mother-infant pairs and 1 infant). Sixteen had received zidovudine only. Six children had an uncertain history of PMTCT. Only 1 child was breast-fed.

Twenty-five children were started on the nevirapine-based regimen. One child was started on the efavirenz-based regimen because of elevated liver enzyme levels at baseline. Of the 25 children on the nevirapine-based regimen, 3 (12%) developed severe adverse reactions to nevirapine within the first 2 weeks. They were subsequently switched to the efavirenz-based regimen.

One 6-month-old infant (4%) died of immune reconstitution syndrome 9 weeks after HAART initiation. The other 25 children had clinical information for at least 48 weeks after initiation of HAART. None developed any AIDS-related events. The mean CD4 cell percentage significantly increased from baseline to week 24 of treatment and thereafter. At week 48 and week 96, 73% (19/26) and 75% (15/20) of children had CD4 cell percentages ≥25%, respectively.

At week 48, 19 (73%) had virologic suppression, 6 children (23%) had virologic failure, and 1 (4%) died. After week 48 there was no additional child with virologic failure. Five of 6 children with virologic failure were found to have poor adherence to the drug regimen compared with 3 in 20 children without failure (P < 0.01). The NNRTI-based regimen was switched to a protease inhibitor-based regimen in 5 children at the median time of 56 weeks (range, 35–96 weeks). One other child was scheduled to switch after further adherence counseling.

Stored plasma samples before HAART initiation of 16 children were available for genotypic resistance assay. None had resistance mutation to NRTIs. Three (20%) had resistance mutation to NNRTI (Y181C in 2, K103N in 1). None of them had confirmed history of nevirapine exposure as a part of PMTCT regimen. All 3 had virologic failure, compared with 2 of 13 (15%) of children without resistance mutation (P < 0.01). These 3 children started HAART at the age of 7.6, 10.0, and 11.3 months, respectively.

DISCUSSION

Our study demonstrated the efficacy of NNRTI-based HAART regimens in children aged 2 years or less. Seventy-three percent of children achieved virologic suppression at week 48. After week 48 there was no additional patient with virologic failure. The median CD4 cell percentage increased from 17% at baseline to 37% at week 96. Seventy-three and 75% of children had immune recovery at week 48 and week 96, respectively.

The mortality of children in our cohort was 4%. It was comparable with the 6% mortality reported from a large multicenter study among HIV-infected children younger than 5 years of age in Africa and Asia.8 In another study from South Africa, the mortality in the group that had criteria for HAART initiation similar to our study was 16%.9 However, in that study HIV infection was diagnosed before 12 weeks of age, whereas the median age of diagnosis was 9.6 months in our study. Infants with

### TABLE 1. Treatment Characteristics of 26 Children Receiving NNRTI-Based Highly Active Antiretroviral Therapy

<table>
<thead>
<tr>
<th>Time After HAART Initiation</th>
<th>No. Children</th>
<th>Weight-for-Age z Score</th>
<th>P</th>
<th>Height-for-Age z Score</th>
<th>P</th>
<th>CD4 Cell Percentage</th>
<th>P</th>
<th>No. Children With Virologic Suppression (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>26</td>
<td>−2.49 (1.60)</td>
<td>−2.19 (1.92)</td>
<td>17 (9)</td>
<td>0/26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24</td>
<td>25</td>
<td>−1.68 (1.14)</td>
<td>&lt;0.01</td>
<td>−2.50 (1.43)</td>
<td>0.27</td>
<td>26 (10)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Week 48</td>
<td>24</td>
<td>−1.09 (1.21)</td>
<td>&lt;0.01</td>
<td>−1.81 (1.25)</td>
<td>0.32</td>
<td>31 (9)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Week 72</td>
<td>19</td>
<td>−0.76 (0.83)</td>
<td>&lt;0.01</td>
<td>−1.52 (1.24)</td>
<td>&lt;0.01</td>
<td>34 (8)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Week 96</td>
<td>15</td>
<td>−0.60 (0.61)</td>
<td>&lt;0.01</td>
<td>−1.08 (0.95)</td>
<td>&lt;0.01</td>
<td>37 (7)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

Data are in mean (SD). P value represents comparison to baseline.

*Virologic suppression was defined as plasma HIV RNA level <400 copies/mL.

1One child died from immune reconstitution syndrome.

2NNRTI-based was switched to PI-based HAART (1).

3NNRTI-based was switched to PI-based HAART (2), staggered enrollment (3).

4Staggered enrollment (3).

5NNRTI-based was switched to PI-based HAART (1), staggered enrollment (3).

6**Staggered enrollment (3).
severe HIV disease may have died before seeking medical treatment. This might explain the lower mortality in our study.

After HAART initiation the mean weight z scores and height z scores increased significantly to catch up with normal children of the same age and gender by 24 and 72 weeks, respectively. In our study, >70% of children achieved CD4 cell percentage ≥25% at week 72 of treatment, whereas the median CD4 cell percentage at treatment initiation was only 17%. This was comparable with a study from 14 developing countries, where 62% of children under the age of 5 years achieved a CD4 cell percentage ≥25% at month 12 of treatment with NNRTI-based HAART regimen. Seventy-nine percent of the patients in this study had the baseline CD4 cell percentage <15%.7

Seventy-three percent of our patients achieved viral suppression at week 48 of treatment. This is comparable with that of a Belgian cohort of 17 infants <2.5 months of age, where 71% achieved viral suppression at week 48.12 The efficacy in our cohort is better than that from several earlier studies in HIV-infected young children, most of whom received a nevirapin-based regimen, where only 50% to 59% achieved viral suppression.1–7

There was a concern regarding the efficacy of NNRTI-based regimen among infants previously exposed to nevirapine as part of PMTCT due to resistance mutation.9 In our study, 3 infants had baseline nevirapine resistance. Most of our patients were referred from outlying hospitals where record keeping was suboptimal. Therefore, although there was no history of nevirapine exposure as part of PMTCT in these 3 infants, unrecorded exposure could not be ruled out. All 3 children had poor virologic outcomes.

The rate of severe adverse drug reactions from nevirapine is 12% (3/25 children) in this study. This was higher than the 5% previously reported in older (median, 7.7 years) HIV-infected Thai children.10 Treatment of HIV-infected children in resource-limited settings is difficult. Choices of antiretroviral drugs are limited because of the high cost of some drugs. Pediatric liquid formulations post logistic problems of short expiration date as well as transport and storage difficulty. Even when available, the dosage schedule may be too complicated for the caregivers. Chiang Mai University was among the pioneer institutes which took the practical approach of prescribing divided adult FDC antiretroviral tablets to these children.10 Because the ratio of drugs in this FDC is fixed and designed for adult dosing, there is a concern for the possibility of under- or over-dosing of 1 component while trying to strictly follow the dosage recommendation of the other component of the FDC.14,15 However, the alternative is to not give any HAART treatment at all. For similar practical reasons, we have used efavirenz to treat our children who have adverse reaction to nevirapine even though it has not yet been licensed for children <3 years of age.

Despite the constraint mentioned above, NNRTI-based HAART in children aged 2 years or less is safe and effective. However, the virologic outcome in subgroups of children who had poor adherence and/or resistance mutation to NNRTI before antiretroviral treatment is poor. Adherence counseling is mandatory and NNRTI-resistance testing before NNRTI-based HAART initiation in Thai infants should be considered.

REFERENCES


MOLLICUTE INFECTIONS IN NEONATES

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Abstract: Mollicutes can cause a wide spectrum of disease, especially in neonates. To better define their disease spectrum in the United States, we reviewed the results of >14,000 mollicute isolates, including 1346 from neonates. When mollicute infection is suspected, clinicians should alert laboratories, which will optimize methods of detection.

Key Words: Ureaplasma, Mycoplasma, mollicute, neonates

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The mollicutes, Ureaplasma spp. and Mycoplasma spp., are significant causes of genitourinary disease in adults1 and neonatal infection.2 The clinical spectrum of disease in neonates...